UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,870	03/18/2005	Jeffrey MC Kenna	PC/4-32611A	4399

75074 7590 11/28/2008

NOVARTIS INSTITUTES FOR BIOMEDICAL RESEARCH, INC.
400 TECHNOLOGY SQUARE
CAMBRIDGE, MA 02139

EXAMINER	
MURRAY, JEFFREY H	
ART UNIT	PAPER NUMBER
1624	
MAIL DATE	DELIVERY MODE
11/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/523,870	KENNA, JEFFREY MC	
	Examiner	Art Unit	
	JEFFREY H. MURRAY	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28 and 31-49* is/are pending in the application.

4a) Of the above claim(s) *39-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28, 31-38, 46-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 28-38 and 46-49 are pending in this application. Claims 1-27 have been cancelled. Claims 39-45 are withdrawn. This action is in response to the applicants' amendment and reply filed August 14, 2008 to a non-final office action.

Withdrawn Rejections/Objections

2. Applicant is notified that any outstanding rejection/objection that is not expressly maintained in this office action has been withdrawn or rendered moot in view of applicant's amendments and/or remarks.

Claim Rejections - 35 USC § 112, 1st paragraph

3. Claims 28, 31-37 and 46-49 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a compound or composition or a pharmaceutically acceptable salt thereof where R_{1a} is an aryl group, does not reasonably provide enablement for a compound, composition, or pharmaceutically acceptable salt where R1a can be a "monocyclic or bicyclic heteroaryl." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Applicant's arguments with respect to the R_{1a} group, R_6 and R_7 group have not been found persuasive. Claims 28-37 and 46-49 are rejected because they contain either the term "heteroaryl" or "heterocyclyl." As seen in the 112, 2nd paragraph rejections, these terms are vague and indefinite. In the argument, examiner stresses

that as currently written, the terms could be interpreted to include over one hundred different ring systems. In that same context, the claims cannot be considered enabled when examiner does not know whether the applicant's intent for "heteroaryl" is a small monocyclic ring such as a thiophene or a larger bicyclic ring such as a triazolopyrazine. Until this is corrected, the claim stands as non–enabled since it is impossible to determine what ring systems are intended. Examiner believes that in properly remedying the 112, 2nd paragraph argument, the 112, 1st paragraph rejection "may" be satisfied as well.

4. Claim 48 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition or a pharmaceutically acceptable salt thereof, does not reasonably provide enablement for any other compositions combined with "an anti-obesity agent, anti-hypertensive agent, inotropic agent or a hypolipidemic agent". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

5. The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation. (*United States v. Teletronics Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based on a single factor, but rather a conclusion reached by weighing many factors (See *Ex parte Forman* 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988).

1) *Amount of guidance provided by Applicant.* While the Applicant has demonstrated within the application how to make 7,8-dihydro-imidazo[1,5-a]pyrazin-6-ones, applicant has provided no guidance, or provided any chemical or biological data and/or testing results of these particular compositions in combination with "an anti-obesity agent, anti-hypertensive agent, inotropic agent or a hypolipidemic agent" or a pharmaceutically acceptable salt thereof.

The quantity of experimentation needed to make or use the invention must be considered to determine if undue experimentation is present. Here applicants do not describe in any explicit detail what types of further active compounds have been combined with the compositions. As currently written, these "medicament active ingredients" could cover a plethora of various disciplines as the "medicament active ingredients" term is undefined.

2) Unpredictability in the art. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. (USPQ 18, 24 (CCPA 1970). See *In re Fisher*, 427 F.2d 833, 839, 166.

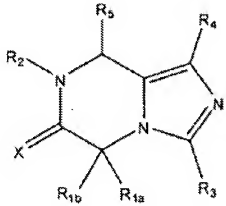
Applicants have provided no chemical synthesis or biological testing of any results where the compositions were combined with these additional "active compounds." Without this, one cannot simply infer that the results of the combination would be additive from the compositions or the active compounds alone. In many instances, the systematic screening of combinations of small molecules can reveal unexpected interactions between the pathways on which they act. (Borisy, et. al.,

Proceedings of the National Academy of Sciences of the United States of America, 100(13) 7977-7982.)

3) *Number of working examples.* The compound core depicted with specific substituents represent a narrow subgenus for which applicant has not provided sufficient guidance to make and use. In addition, this disclosure is not sufficient to allow extrapolation of the limited examples to enable the scope of the compounds instantly claimed or preventive agents. Applicant has provided no working examples of any compounds, compositions or pharmaceutically acceptable salts in the present application.

Within the specification, "specific operative embodiments or examples of the invention must be set forth. Examples and description should be of sufficient scope as to justify the scope of the claims. *Markush* claims must be provided with support in the disclosure for each member of the *Markush* group. Where the constitution and formula of a chemical compound is stated only as a probability or speculation, the disclosure is not sufficient to support claims identifying the compound by such composition or formula." See MPEP 608.01(p).

4) *Scope of the claims.* The scope of the claims involves all of the thousands of compositions of the following formula:



and the compound above is combined with an "an anti-obesity agent, anti-hypertensive agent, inotropic agent or a hypolipidemic agent" thus the scope of the claims is broad.

5) *Nature of the invention.* This invention is directed generally to compounds which are inhibitors of the P450 enzyme aldosterone synthase, and, thus, may be employed for the treatment of aldosterone mediated conditions.

6) *Level of skill in the art.* The artisan using Applicants invention would be a chemist with a M.S. pr Ph.D. in chemistry, and having several years of bench experience.

MPEP §2164.01 (a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here that Applicant is not enabled for treating the disease mentioned.

Claim Rejections - 35 USC § 112, 2nd paragraph

6. Claims 28, 31-38 and 46-49 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. The scope of "heteroaryl" and "heterocyclyl" still requires clarification. Applicants have not defined these terms with reasonable clarity. The terms are defined with non-limiting examples making them impossible to pin down. For example, when one states C_1-C_4 alkyl, there are a small finite number of possibilities that exist in that set. One ordinarily skilled in the art realizes and understands this. However when one states, "heteroaryl" and then provides a list of well over 50 examples and states the list is non-limiting, how can this be considered definite? One skilled in the art could instantly envision well over one hundred ring systems that qualify under this broad, vague definition. Does the applicant wish to claim a thiophene or a pyrazolopyrimidine? Applicant must narrow such broad terminology by either eliminating such a broad definition or by inserting the specific ring systems they wish to cover into the claim themselves.

In addition, the argument against "optionally substituted" also falls under this same argument. In the absence of the specific moieties intended to effect modification by "substitution" or attachment to the chemical core claimed, the term "optionally substituted" renders the claim in which it appears indefinite in all occurrences where the applicant fails to articulate by chemical name, structural formula or sufficiently distinct functional language, the particular moieties applicant regards as those which will

facilitate substitution, requisite to identifying the composition of matter claimed. Applicants have cited *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385 (Fed. Cir. 1987). However in their arguments they state, "In the present case, whenever the term 'substituted' is recited in the claim language, the term is followed by specific definitions, groups or elements. In other words, the term 'substituted' modifies a distinct set of possibilities clearly defined in the claims and supported by the specification." In the present case the exact opposite is true. "Substituted" is a vague and indefinite term because there is no "...set of possibilities clearly defined in the claims and supported by the specification." The same argument can be used for an example such as "optionally substituted heteroaryl," whereby one skilled in the art would have no idea whatsoever what type of compound applicant was trying to claim with such ambiguous claim language. The arguments have not been found persuasive. The rejection is maintained. No new matter permitted. Appropriate correction is required.

8. Claims 47 and 49 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. The recitation of an intended use, chemical activity, or functional description of some "additional" property for a compound (or moiety/functionality attached to a chemical core) or a composition containing same in a dependent claim, must result in a tangible structural difference between the product and of the independent claim and the product set forth in the dependent claim. In the absence of said structural difference between the product of the independent claim and that of the dependent claim, said

dependent claim is seen to be a substantial duplicate, and said recitation is not afforded critical weight and fails to further limit the product in said dependent claim. In the instant set of claims, claims 47 and 49 fail to further limit the claims to compositions from which they depend.

Allowable Subject Matter

Claim 38 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim 38 is free of the prior art. The closest prior art to claim 38 is Yoden, et. al., WO 9700257, which teaches an identical core compound, however a fluorene group is the R1a group, which is not aromatic, and therefore is not considered an aryl group.

Conclusion

10. Claims 28, 31-38 and 46-49 are rejected.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey H. Murray whose telephone number is (571) 272-9023. The examiner can normally be reached on Mon.-Thurs. 7:30-6pm EST.

12. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey H Murray/
Patent Examiner
Art Unit 1624

/James O. Wilson/
Supervisory Patent Examiner, Art Unit 1624